The SAFER Trial

*"**S**aphenous Vein Graft **A**ngioplasty **F**ree of **E**mboli **R**andomized"*

Evaluation of the Clinical Safety and Efficacy of the PercuSurge GuardWire in Saphenous Vein Graft Intervention

Donald S. Baim, MD FACC
Harvard Medical School
Brigham and Women's Hospital

Personal Financial Disclosure

From the inception of the SAFER Trial in September 1998 to the current date, I have not had any equity interest, either in stock options or stock ownership, in PercuSurge, Inc.

The SAFER Trial

Background

The average longevity of a vein graft is 8-10 years

- 40% occlude
- 75% develop severe narrowing

Vein graft atherosclerosis is diffuse and friable

- Intervention may cause distal embolization
- Embolization compromises the distal microcirculation
- Manifests as no-reflow (8-10%) and CK elevation (17-20%)
- Mortality of 3.4% at 30 days (14% with CK-MB > 3x normal)

A device that could capture and remove embolic particles before they reach the myocardium could reduce these complications

The SAFER Trial

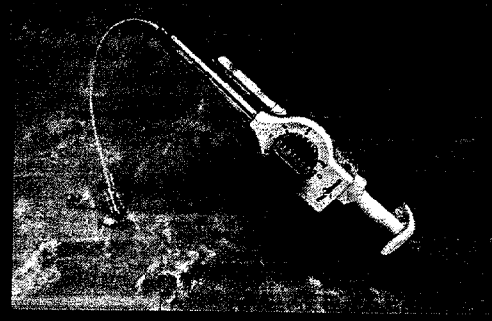
PercuSurge GuardWire® System

The SAFER Trial

PercuSurge GuardWire® System

4 components:

- GuardWire Plus®
- MicroSeal® Adapter
- EZ-Flator™
- Export® Catheter



The SAFER Trial

Prior GuardWire Registries:

Webb et al (*JACC 34:461, 1999*)

- single site registry of 24 patients, 27 lesions
- MACE - 3.7%

SAFE (TCT 1999, *E. Grube*)

- 103 patient European registry (7 sites)
- visible material removed in 95% of cases
- 81% of material is under 96 microns
- MACE - 4.9%

The SAFER Trial

The SAFER trial was designed as a prospective randomized trial to determine if the GuardWire reduced the incidence of MACE, compared to the conventional standard of care (unprotected stenting).

The SAFER Trial

Study Management

Study Coordination:	**Cardiovascular Data Analysis Center (CDAC)** Boston, MA
QCA Core Lab:	**Brigham and Women's Angiographic Core Laboratory (CDAC)** Boston, MA
ECG Core Lab:	**Cardiovascular Data Analysis Center (CDAC)** Boston, MA
Study Monitoring:	**Bailer Monitoring** Lake Hopatcong, NJ
Sponsor:	**PercuSurge, Inc.** Sunnyvale, CA

The SAFER Trial
Study Design

Primary Endpoint: "Major Adverse Clinical Events" (MACE) out to 30 Days

A combined clinical endpoint defined as:

- Death
- Q wave MI
- Non Q-Wave MI (CK-MB > 3x ULN)
- Emergent bypass surgery
- Repeat target vessel revascularization

The SAFER Trial
Study Design

Inclusion criteria

Lesions (50-99%) in SVG's 3-6 mm in diameter
More than 5 mm from ostium; 20 mm from distal anastomosis
At least TIMI 1 flow at baseline

Exclusion criteria

Ongoing MI with + CK-MB
Ejection Fraction < 25%
Serum Creatinine > 2.5 unless on hemodialysis
Planned use of atherectomy device

The SAFER Trial
Study Design

Enrollment

801 patients:

- 142 initial patients (diffuse disease excluded)
- 659 enrolled with inclusion of diffuse disease
  - 551 cohort pre-specified interim analysis → DSMB
  - 108 additional patients enrolled before study terminated

The SAFER Trial
Baseline Demographics (n=659)

	GuardWire (n=334)	No GuardWire (n=325)
Age (yrs)	**68.3 (36, 90)**	**68.6 (45, 92)**
Male	**81.1%**	**84.0%**
History Diabetes Mellitus	**31.7%**	**34.5%**
Prior MI	**59.0%**	**62.9%**
Prior CVA/TIA	**10.2%**	**13.1%**
↑ Exertional Angina	**40.2%**	**39.4%**
CCS III or IV	**74.8%**	**72.9%**
Rest Angina	**39.0%**	**37.5%**
Triple Vessel Disease	**74.0%**	**79.3%**
Ejection Fraction Mean	**47.9%**	**47.2%**

The SAFER Trial

Baseline Lesion Characteristics (n=659)

	GuardWire	No GuardWire
Pre RVD (mm)	**3.45** (1.99, 5.73)	**3.42** (1.54, 6.48)
MLD (mm)	**1.10** (0.00, 3.58)	**1.07** (0.00, 3.08)
Diameter Stenosis	**69.0%**	**70.1%**
Lesion Length	**15.73** (2.16, 76.99)	**16.74** (3.00, 79.29)
Target Vessel		
SVG-LAD	**20.6%**	**17.3%**
SVG-LCX	**43.7%**	**40.5%**
SVG-RCA	**35.4%**	**42.3%**
Thrombus	**37.8%**	**39.9%**
Eccentric Lesion	**40.2%**	**35.4%**
Angulation >45%	**6.8%**	**6.0%**

The SAFER Trial

Technical and Procedural Success

Technical Success was defined, according to the IFU, as:

- Successful delivery of the GuardWire to the intended target site
- Inflation of the occlusion balloon
- Aspiration using the Export catheter
- Balloon deflation

Procedural Success was defined as:

- Achievement of a final diameter stenosis < 50%
- No in-hospital MACE

The SAFER Trial

Technical and Procedural Success (n=659)

	GuardWire	No GuardWire
Technical Success	91.6%	n/a
Procedure Success	90.7%	84.0%
Number of Stents	1.4	1.3

The SAFER Trial Results

MACE at Index Hospitalization (n=659)

	GuardWire (n=334 Pts)	No GuardWire (n=325 Pts)	
All Myocardial Infarction	**7.8%**	**15.1%**	***p=.003***
Q Wave MI	**1.2%**	**1.5%**	***NS (p=.749)***
Non Q-Wave MI	**6.6%**	**13.8%**	***p=.003***
Death	**0.6%**	**1.2%**	***NS (p=.445)***
Emergent CABG	**0.0%**	**0.6%**	***NS (p=.243)***
TLR	**0.3%**	**0.9%**	***NS (p=.367)***
MACE @ Index	**8.1%**	**15.7%**	***p=.001***

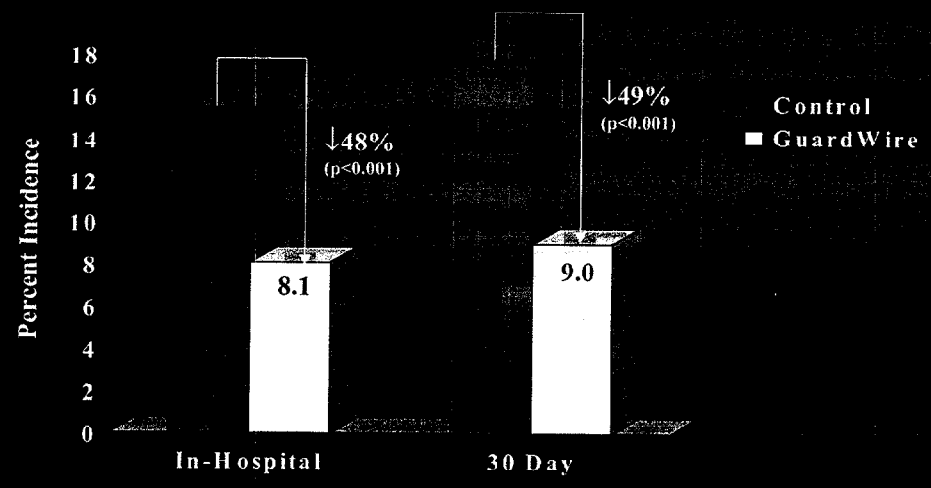
The SAFER Trial Results

Primary Endpoint: MACE out to 30 days (n=659)

	GuardWire (n=334 Pts)	No GuardWire (n=325 Pts)	
All Myocardial Infarction	8.1%	15.7%	*p=.003*
Q Wave MI	1.2%	1.5%	*NS (p=.749)*
Non Q-Wave MI	6.9%	14.5%	*p=.003*
Death	0.9%	2.8%	*NS (p=.086)*
Emergent CABG	0.0%	0.6%	*NS (p=.243)*
TLR	0.6%	2.5%	*NS (p=.060)*
MACE Out to 30 Days	9.0%	17.8%	*p=.001*

The SAFER Trial Results

MACE (n=659)



The SAFER Trial Results

Secondary Endpoints (n=659)

Post-Procedure TIMI Flow:

	GuardWire	No GuardWire	
TIMI 0, 1	1.5%	0.6%	*NS (p=.451)*
TIMI 2	0.9%	4.5%	*p=.004*
TIMI 3	97.6%	94.9%	*NS (p=.070)*
No-reflow	3.3%	8.3%	*p=.005*
Perforation	0.3%	1.5%	*NS*
Dissection	2.4% *All type A and B*	0.9%	*NS (p=.223)*
Subac. Closure	0.9%	1.8%	*NS (p=.334)*

The SAFER Trial Results

GP *IIb/IIIa Use (n=659)*

GP IIb/IIIa inhibitors were used in >60% in both arms, predominately before intervention

PercuSurge had MACE benefit with or without their use

	GuardWire	No GuardWire	
IIb/IIIa	10.1%	20.8%	*p=.003*
No IIb/IIIa	7.1%	12.4%	*p=.051*

Why? GP IIb/IIIa's prevent platelet thrombi, but they do *not* dissolve atherosclerotic plaque.

The SAFER Trial
Study Design

Enrollment

801 patients:

- 142 initial patients (diffuse disease excluded)
- 659 enrolled with inclusion of diffuse disease
  - 551 cohort pre-specified interim analysis → DSMB
  - 108 additional patients enrolled before study terminated

The SAFER Trial Results
MACE out to 30 days

659 Patients	**GuardWire (n=334 Pts)**	**No GuardWire (n=325 Pts)**	
MACE Out to 30 Days	**9.0%**	**17.8%**	***p=.001***
801 Patients	**GuardWire (n=406 Pts)**	**No GuardWire (n=395 Pts)**	
MACE Out to 30 Days	**9.6%**	**16.5%**	***p=.004***

The SAFER Trial Conclusions

The PercuSurge GuardWire® System proved Safe and Effective in

- Recovering embolic material
- Preserving normal flow
- Reducing MACE by ~50%

during the percutaneous interventional treatment of saphenous vein bypass grafts

The SAFER data underscores the importance of using the GuardWire System during SVG intervention